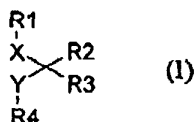


*New Title*  
Please amend the application as follows:

*el 13*  
*per amle*  
In the claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application.

*el 16*  
*susceptible to*  
*off much*  
1. (currently amended) A compound of general Formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

*OK as per Sudash 4/14/04*  
*still includes virtually all Hets*  
*all right*  
 $\textcircled{R_1}$  is selected from the group consisting of:

$\text{C}_1\text{--}\text{C}_6$ ,  $\text{C}_2\text{--}\text{C}_6$  alkyl, substituted with one or more basic groups; cycloalkyl, substituted with one or more basic groups; heterocyclyl, comprising at least one nitrogen atom; heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups; and aryl, substituted with one or more basic groups;

$\textcircled{R_2}$  is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino,  $\textcircled{\text{aryl}}$ , carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol,  $\text{Z}_2\text{N--CO--O--}$ ,  $\text{ZO--CO--NZ--}$ , and  $\text{Z}_2\text{N--CO--NZ--}$ ; *COOH*

$\textcircled{R_3}$  is selected from the group consisting of  $\text{COOR}_5$ ,  $\text{SO}(\text{OR}_5)$ ,  $\text{SO}_3\text{R}_5$ ,  $\text{P=O}(\text{OR}_5)_2$ ,  $\text{B}(\text{OR}_5)_2$ ,  $\text{P=OR}_5(\text{OR}_5)$ , tetrazole, and a carboxylic acid isostere; *COOH*

$\textcircled{R_4}$  represents a  $\begin{array}{c} \text{O}-\text{R}_5 \\ | \\ \text{P}-\text{R}_6 \\ | \\ \text{O} \end{array}$  -group, or a  $\begin{array}{c} \text{O} \\ || \\ \text{N}-\text{OH} \\ | \\ \text{R}_7 \end{array}$  -group, or a  $\begin{array}{c} \text{O} \\ || \\ \text{C}-\text{R}_5 \end{array}$  -group,

$R_5$  is H,  $C_1-C_6$  alkyl, or aryl;

$R_6$  is  $C_1-C_6$  alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

$H_2N-C(Z)-CONH-C(Z)-$  or  $H_2N-C(Z)-$  group;

$R_7$  is H or  $C_1-C_6$  alkyl;

X is selected from the group consisting of O, S, SO,  $SO_2$ ,  $C(Z)_2$ ,  $N(Z)$ ,  $NR_7SO_2$ ,  $SO_2NR_7$ ,  $NR_7CO$ , and  $CONR_7$ ;

Y is selected from the group consisting of O,  $N(Z)$ , S,  $C(Z)_2$ , and a single bond; and

Z is independently selected from the group consisting of H,  $C_1-C_6$  alkyl, aryl, cycloalkyl, and heterocyclyl,

with the proviso that when X is O, S, SO,  $SO_2$ ,  $N(Z)$ ,  $NR_7SO_2$ ,  $SO_2NR_7$ , or  $NR_7CO$ , then Y is  $C(Z)_2$  or a single bond.

2. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

$R_1$  is selected from the group consisting of:

cycloalkyl, substituted with one or more basic groups ;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

$R_2$  is selected from the group consisting of H,  $C_1-C_3$  alkyl, amino, halogen, and hydroxy;

$R_3$  is  $COOR_5$ ;

$R_4$  represents a  $\begin{array}{c} \text{O}-R_5 \\ | \\ -\text{P}-R_6 \\ || \\ \text{O} \end{array}$  -group,

$R_5$  is H,  $C_1-C_6$  alkyl, or aryl;

$R_6$  is  $C_1-C_6$  alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

$H_2N-C(Z)-CONH-C(Z)-$  or  $H_2N-C(Z)-$  group;

X is  $C(Z)_2$ ;

Y is O or  $C(Z)_2$ ; and

Z is independently H or  $C_1-C_6$  alkyl.

3. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

$R_1$  is selected from the group consisting of:

cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

$R_2$  is selected from the group consisting of H,  $C_1-C_3$  alkyl, amino, halogen, and hydroxy;

$R_3$  is  $COOR_5$ ;

$R_4$  represents a  $\begin{array}{c} \text{O} \\ || \\ \text{C}-\text{N}-\text{OH} \\ | \\ R_7 \end{array}$  -group,

$R_5$  is H,  $C_1-C_6$  alkyl, or aryl;

$R_7$  is H or  $C_1-C_6$  alkyl;

X is  $C(Z)_2$ ;

Y is C(Z)<sub>2</sub> or a single bond; and  
Z is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

4. (previously presented) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R<sub>1</sub> is selected from the group consisting of:

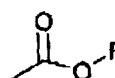
cycloalkyl, substituted with one or more basic groups;

heterocyclyl, comprising at least one nitrogen atom; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups;

R<sub>2</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, and hydroxy;

R<sub>3</sub> is COOR<sub>5</sub>;

R<sub>4</sub> is a -R<sub>5</sub>-group;


R<sub>5</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, or aryl;

X is C(Z)<sub>2</sub>;

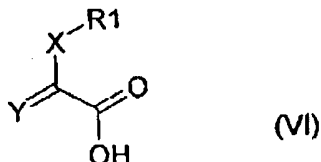
Y is C(Z)<sub>2</sub> or a single bond; and

Z is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

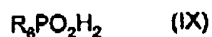
5. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein R<sub>1</sub>, R<sub>5</sub>, R<sub>6</sub>, and Z are as defined in claim 1, R<sub>2</sub> is H, R<sub>3</sub> is COOR<sub>5</sub>,

R<sub>4</sub> represents a -group.

X is C(Z)<sub>2</sub>, and Y is C(Z)<sub>2</sub>,  
comprising the step of:  
reacting a compound of Formula VI,

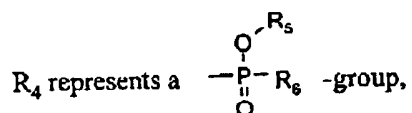


wherein R<sub>1</sub> and Z is as defined in claim 1, X is C(Z)<sub>2</sub>, and Y is C(Z)<sub>2</sub>, with a compound of Formula IX,

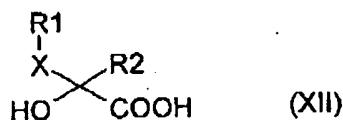


wherein R<sub>6</sub> is as defined in claim 1, in the presence of a reagent, under standard conditions.

6. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>5</sub>, R<sub>6</sub>, and Z are as defined in claim 1, R<sub>3</sub> is COOR<sub>5</sub>, X is C(Z)<sub>2</sub>, Y is O, and



comprising the step of:  
reacting a compound of Formula XII,



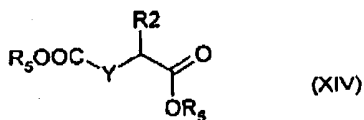
wherein  $R_1$  and  $R_2$  are as defined in claim 1 and X is  $C(Z)_2$ , with a compound of Formula XIII,



wherein  $R_6$  is as defined in claim 1, in the presence of a coupling reagent under standard conditions.

7. (currently amended) A process for the preparation of a compound according to any one of claims 1-4,

wherein  $R_1$  and  $R_2$  are as defined in claim 1, X is  $C(Z)_2$ , and Y is are independently  $C(Z)_2$  or a single bond, and  $R_3$  and  $R_4$  are  $COOR_5$ , comprising the step of:  
reacting a compound of Formula XIV,

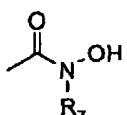


wherein  $R_2$  and  $R_5$  are as defined in claim 1, and Y is  $C(Z)_2$  or a single bond, with a compound of the general Formula III,

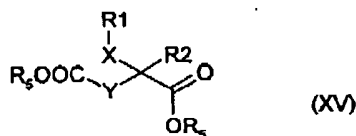


wherein  $R_1$  is as defined in claim 1, X is  $C(Z)_2$ , and L is a leaving group, in the presence of a base, under standard conditions.

8. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein  $R_1$ ,  $R_2$ ,  $R_5$ ,  $R_7$ , X, Y and Z are as defined in claim 1,  $R_3$  is  $\text{COOR}_5$  and

$R_4$  represents a  -group,

comprising the step of:  
reacting a compound of Formula XV,



with a compound of Formula XVI,



wherein  $R_7$  is as defined in claim 1, in the presence of a reagent under standard conditions.

9. (previously presented) A pharmaceutical formulation comprising a compound according to any one of claims 1-4 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

10. (cancelled)

11. (cancelled)

12. (previously presented) A method for the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1-4.

13. (previously presented) A pharmaceutical formulation for the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound according to any one of claims 1-4 in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

14. (previously presented) A pharmaceutical formulation, comprising:

- (i) a compound of Formula I as defined in claim 1 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; and
  - (ii) one or more antithrombotic agents with a different mechanism of action from that of component (i),
- in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

15. (previously presented) A kit of parts comprising:

- (i) a pharmaceutical formulation comprising a compound of Formula I as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) a pharmaceutical formulation comprising one or more antithrombotic agents with a different mechanism of action from



that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier;  
wherein compound (i) and agent (ii) are each formulated for administration in conjunction with the other.

16. (previously presented) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) one or more antithrombotic agents with a different mechanism of action from that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

17. (previously presented) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation from the kit of claim 15.

18. (previously presented) The compound according to any one of claims 1-4, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.

19. (previously presented) The process according to claim 5, wherein the reagent is N,O-bis(trimethylsilyl)acetamide (BSA) or hexamethyldisilazane (HMDS).
20. (previously presented) The process according to claim 6, wherein the coupling reagent is selected from the group consisting of:
  - (i) dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP);
  - (ii) (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBop)/ diisopropylethylamine (DIPEA); and
  - (iii)  $\text{SOCl}_2$ .
21. (previously presented) The process according to claim 7, wherein the leaving group is selected from the group consisting of Cl, Br, I, and tosyl.
22. (previously presented) The process according to claim 7, wherein the base is lithium diisopropylamide (LDA) or NaH.
23. (previously presented) The process according to claim 8, wherein the reagent is dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP).
24. (previously presented) The formulation according to claim 14, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor ( $\text{P}_2\text{T}$ ) antagonist.

25. (previously presented) The kit according to claim 15, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor ( $P_2T$ ) antagonist.
26. (previously presented) The method according to claim 16, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor ( $P_2T$ ) antagonist.